MeCP2 is required for major satellite forward transcript recruitment at pericentric heterochromatin during neural differentiation

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The methyl-CpG binding protein 2 (MeCP2) is a ubiquitous transcription factor predominantly expressed in the brain and mutated in Rett syndrome, a progressive neurodevelopmental disorder. Neuronal MeCP2 genome-wide binding tracks methyl-CpG density and its absence results in large-scale changes in chromatin structures, suggesting a global regulatory role. In mouse cells MeCP2 accumulates at pericentric heterochromatin (PCH), composed by major satellite DNA of different chromosomes that aggregate to form chromocenters, structures possibly critical for the establishment of silent compartments. Several proteins and ncRNAs [e.g. HP1s and maj sat forward transcript (MSFT)] are relevant for establishment and maintenance of PCH.
Recently, we highlighted a crucial role of MeCP2 in the PCH re-organization during neural differentiation, supporting the view of MeCP2 as a multifunctional chromatin organizing factor.
To unravel the molecular mechanism by which MeCP2 regulates the PCH re-organization we investigated the spatial distribution of MSFT and HP1s during neural differentiation of wt and MeCP2-/y cells. MSFT expression increases during differentiation of both cell lines with stronger and more numerous RNA-FISH signals in wt compared with MeCP2-/y cells. Moreover, MeCP2 co-localizes and physically associates with MSFT. These data point out a contribution of MeCP2 in the sub-nuclear localization of MSFT. Noteworthy, RNAse treatment causes delocalization of MeCP2 and HP1s from the chromocenters, suggesting a role of RNAs in MeCP2 and HP1s positioning. Furthermore, HP1s co-localize with MeCP2 and MSFT at chromocenters. Our preliminary data allow to speculate that MeCP2 may cooperate with MSFT and HP1s for the PCH organization.